

§ 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

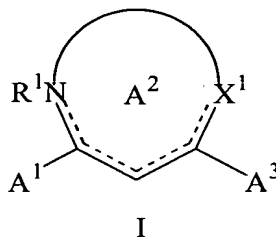
Amendments

In the Claims:

Please cancel claims 15-21 and 41-46 without prejudice or disclaimer.

Please substitute the following claims 1, 5, 6, 14, 22, 28, 36, 48-53, 56-61, 63, 66-70, 72, 73, 75-80, 82, and 86 for the pending claims 1, 5, 6, 14, 22, 28, 36, 48-53, 56-61, 63, 66-70, 72, 73, 75-80, 82, and 86:

1. (once amended) A compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R¹ is hydrogen, (C₁₋₆)alkyl or -C(O)R⁶, wherein R⁶ is as defined below, or R¹ is absent when a double bond exists between the nitrogen atom to which R¹ is attached and an adjacent ring atom or R¹ is as defined below;

X¹ is -S(O)_n-, wherein n is 0, 1, or 2;

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~~A¹ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A¹ may be substituted with a group selected from -X²R³, -X²OR³, -X²C(O)R³, -X²OC(O)R³, -X²C(O)OR³, -X²SR³, -X²S(O)R³, -X²S(O)₂R³, -X²NR³R⁴, -X²NR⁴C(O)R³, -X²NR⁴C(O)OR³, -X²C(O)NR³R⁴, -X²NR⁴C(O)NR³R⁴, -X²NR⁴C(NR⁴)NR³R⁴, -X²NR⁴S(O)₂R³ and -X²S(O)₂NR³R⁴, wherein X² is a bond or (C₁₋₆)alkylene, R³ is -X²R⁵ wherein X² is as defined above and R⁵ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A¹ and R⁵ that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A¹ and R⁵ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the proviso that only one of A¹ and R⁵ is a fused polycyclic ring system;~~

A² is a monocyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms,

wherein A^2 may be substituted with a group selected from $-X^2R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A^2 and R^8 that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

A^3 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A^3 may be substituted with a group selected from $-X^2R^9$, $-X^2OR^9$, $-X^2C(O)R^9$, $-X^2OC(O)R^9$, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$,

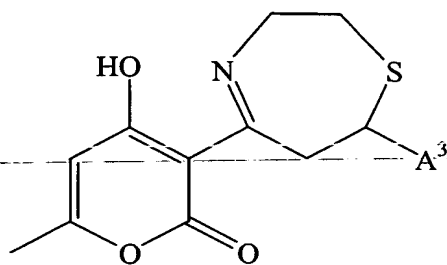
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$-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$,
 $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$; wherein
 X^2 is a bond or (C_{1-6}) alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl
 containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms
 or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each
 containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is
 hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A^3 and R^{10} that
 contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected
 from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$,
 $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$,
 $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$,
 $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is
 (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said carbocycloalkyl and
 heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups
 independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that
 only one of A^3 and R^{10} is a fused polycyclic ring system; and the *N*-oxide derivatives,
 prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of
 stereoisomers; and the pharmaceutically acceptable salts thereof;
 with the proviso that when said compound is Formula II(a):

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II(a)

then A³ is other than:

unsubstituted pyridyl;

unsubstituted thienyl;

unsubstituted indolyl;

unsubstituted phenyl;

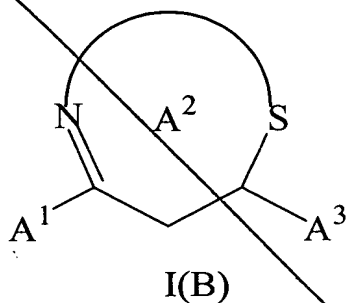
benzo[1,3]dioxolyl;

2,3-dihydro-benzo[1,4]dioxinyl;

phenyl which is mono-substituted by fluoro, bromo, iodo, nitro, methyl, isopropyl, ethoxy or methylsulfanyl; and

phenyl which is substituted by at least one of chloro, hydroxy or methoxy.

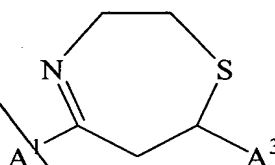
5. The compound of Claim 4 in which said compound is of Formula I(B):



I(B)

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

6. The compound of Claim 5 in which said A^2 is 2,3,6,7-tetrahydro-[1,4]thiazepin-5,7-ylene, that is the compound of Formula I(C):



I(C)

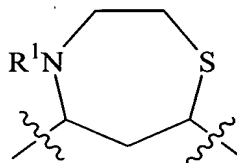
in which said 2,3,6,7-tetrahydro-[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

14. The compound of Claim 13 which is:

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

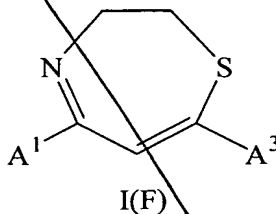
22. The compound of Claim 4 in which said A^2 is a group of Formula (k):



(k)

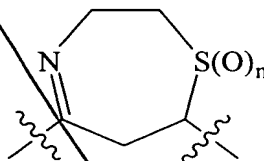
in which said group of Formula (k) may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

28. The compound of Claim 4 in which said A^2 is 2,3-dihydro-[1,4]thiazepin-5,7-ylene that is the compound of Formula I(F):



in which said 2,3-dihydro-[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²C(O)NR⁴X²C(O)OR⁴, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² is a bond or (C₁₋₆)alkylene, R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

36. The compound of Claim 35 in which A² is a group of Formula (I):



(I)

in which said group of Formula (I) may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²C(O)NR⁴X²C(O)OR⁴, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² is a bond or (C₁₋₆)alkylene, R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

48. A compound selected from the group consisting of:

7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-

2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepine-3-carboxylic acid; and

2-((1-[7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-

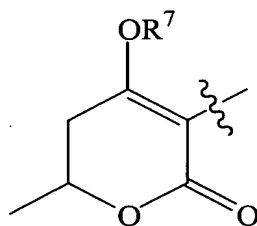
2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepin-3-yl]-methanoyl}-amino)-propionic acid

tert-butyl ester;

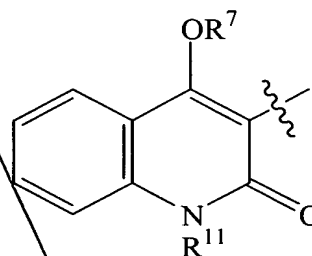
and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

49. The compound of Claim 1 in which A¹ is a group selected from Formulae (b),

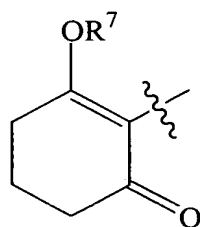
(c), (d), (e) and (f):



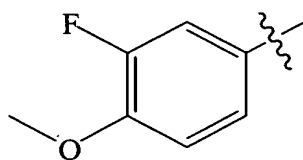
(b)



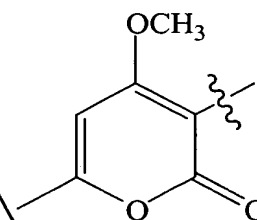
(c)



(d)



(e)



(f)

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valance is attached to A^2 ; and

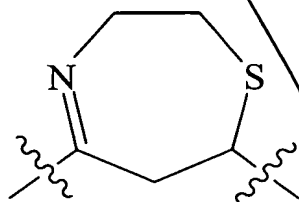
~~A^2 is as defined above or is a monocyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-X^2R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A^2 and R^8 that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and the *N*-oxide~~

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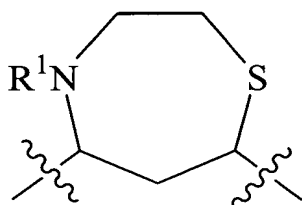
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derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

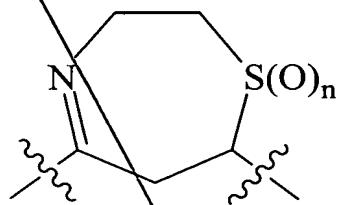
50. The compound of Claim 49 in which A² is a group selected from Formulae (h), (k), (l) and (m):



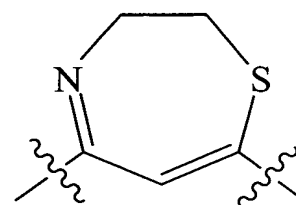
(h)



(k)



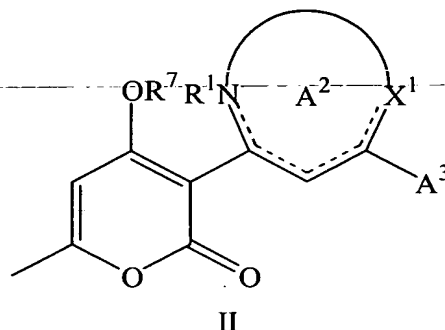
(l)



(m)

in which n is 1 or 2 and R¹ is acetyl or trifluoroacetyl; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

51. A compound of Formula II:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R^1 is hydrogen, (C_{1-6}) alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

R^7 is hydrogen;

X^1 is $-S(O)_n-$, wherein n is 0, 1, or 2;

A^2 is a monocyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted

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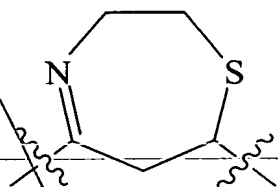
(C_{1-6}) alkyl, wherein each ring within A^2 and R^8 that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

A^3 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2C(O)R^9$, $-X^2OC(O)R^9$, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$, $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A^3 and R^{10} that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected

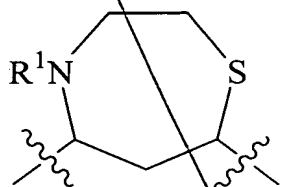
from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A³ and R¹⁰ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo with the proviso that only one of A³ and R¹⁰ is a fused polycyclic ring system; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof;

provided, however, Formula II does not represent a compound wherein A² is 2,3,6,7-tetrahydro-[1,4]thiazepinylene and A³ is benzo[1,3]dioxolyl, indolyl, phenyl, pyridyl or thienyl, wherein said phenyl may be substituted with 1 to 3 groups independently selected from halo, nitro, hydroxy, (C₁₋₄)alkyl, (C₁₋₄)alkylsulfanyl and (C₁₋₄)alkyloxy or any *N*-oxide derivative; protected derivative, individual stereoisomer or mixture of stereoisomers, or pharmaceutically acceptable salt thereof.

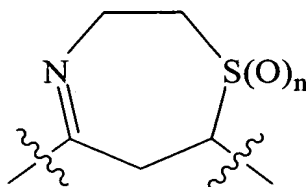
52. The compound of Claim 51 in which A² is a group selected from Formulae (h), (k), (l) and (m):



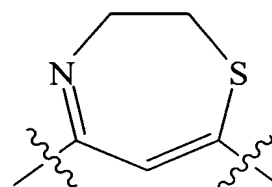
(h)



(k)



(l)



(m)

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

53. The compound of Claim 52 in which A^3 is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6}) alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, halo, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and $-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

AB

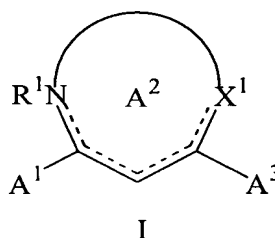
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56. (once amended) The pharmaceutical composition of Claim 55, wherein said cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosphamide, ifosfamide, vincristine, mitoguanzone, epirubicin, aclarubicin, bleomycin, imitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, HERCEPTIN (trastuzumab), RITUXAN (rituximab) and alanosine.

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57. A method of treating a disorder responsive to the induction of apoptosis in an animal suffering said disorder, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R^1 is hydrogen, (C_{1-6}) alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

X^1 is $-S(O)_n-$, wherein n is 0, 1, or 2;

A^1 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and

unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A¹ may be substituted with a group selected from -R³, -X²OR³, -X²C(O)R³, -X²OC(O)R³, -X²C(O)OR³, -X²SR³, -X²S(O)R³, -X²S(O)₂R³, -X²NR³R⁴, -X²NR⁴C(O)R³, -X²NR⁴C(O)OR³, -X²C(O)NR³R⁴, -X²NR⁴C(O)NR³R⁴, -X²NR⁴C(NR⁴)NR³R⁴, -X²NR⁴S(O)₂R³ and -X²S(O)₂NR³R⁴, wherein X² is a bond or (C₁₋₆)alkylene, R³ is -X²R⁵ wherein X² is as defined above and R⁵ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A¹ and R⁵ that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A¹ and R⁵ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the provisos that only one of A¹ and R⁵ is a fused polycyclic ring system;

A² is a monocyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A² may be substituted with a group selected from -R⁸, -X²OR⁸, -X²C(O)R⁸, -X²OC(O)R⁸, -X²C(O)OR⁸, -X²SR⁸, -X²S(O)R⁸, -X²S(O)₂R⁸, -X²NR⁴R⁸, -X²NR⁴C(O)R⁸,

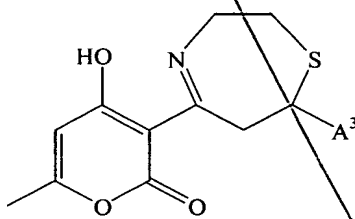
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$-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$,
 $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^8 is $-X^2R^9$
 wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms,
 heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or
 saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms,
 and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted
 (C_{1-6}) alkyl, wherein each ring within A^2 and R^8 that contains from 3 to 8 ring atoms may be
 substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro,
 halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$,
 $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$,
 $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and
 $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or
 halo-substituted (C_{1-6}) alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and
 heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups
 independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that
 only one of A^2 and R^8 is a fused polycyclic ring system; and

A^3 is a monocyclic or fused polycyclic ring system selected from aryl containing a
 total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and
 unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each
 containing a total of 3 to 14 ring atoms, wherein A^3 may be substituted with a group selected
 from $-R^9$, $-X^2OR^9$, $-X^2C(O)R^9$, $-X^2OC(O)R^9$, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$,
 $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$,
 $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein

Handwritten: A³ Sub B¹

X^2 is a bond or (C_{1-6}) alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially-unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A^3 and R^{10} that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A^3 and R^{10} is a fused polycyclic ring system; or an *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof; with the proviso that when said compound is of Formula II(a):



II(a)

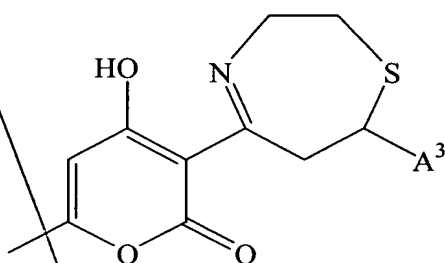
then A³ is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl;

and

- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino.

58. The method of claim 57, with the further proviso that when said compound is Formula II(a):



II(a)

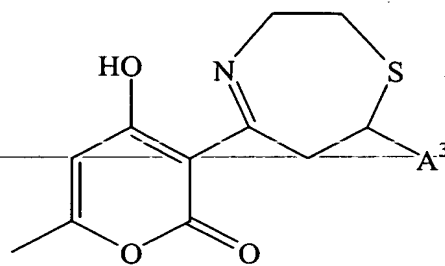
then A³ is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl, or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino.

59. The method of claim 57, with the further proviso that when said compound is Formula II(a):

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II(a)

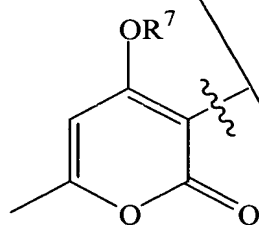
then A^3 is other than:

- (a) benzo[1,3]dioxolyl;
- (b) 2,3-dihydro-benzo[1,4]dioxinyl; and
- (c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C_{1-6}) alkyl.

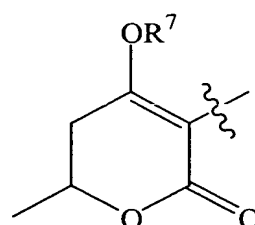
60. The method of Claim 57, wherein A^1 of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):

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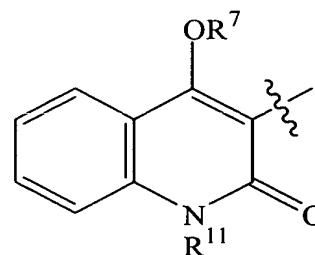
A/10



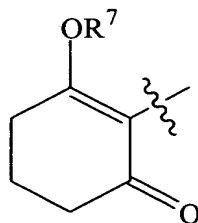
(a)



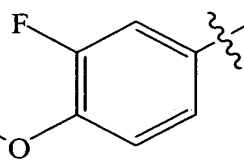
(b)



(c)



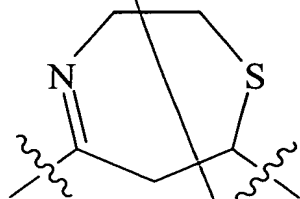
(d)



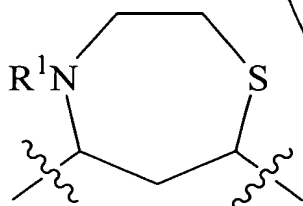
(e)

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valance is attached to A^2 ; and

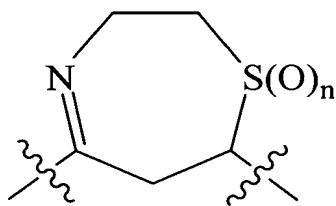
A^2 of said compound is as defined above or is a group selected from Formulae (h), (k), (l) and (m):



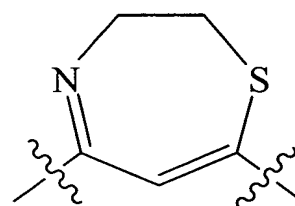
(h)



(k)



(l)



(m)

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl; or an N -oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

61. The method of Claim 60, wherein A^3 of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6}) alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently

selected from (C₁₋₆)alkyl, halo, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²SR⁴, -X²S(O)₂R⁶ and -X²NR⁴R⁴, wherein R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

63. The method of claim 57, wherein said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thiazepin-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1H-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1H-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-
tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-
hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-
hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-
hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-
tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

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~~3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;~~

~~3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;~~

~~3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;~~

~~4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;~~

~~4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;~~

~~4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;~~

~~3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;~~

~~3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;~~

~~3-(7-[2,2']bithienyl-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;~~

~~3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;~~

~~3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;~~

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3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfonyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1H-1λ⁴-[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1H-1λ⁶-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

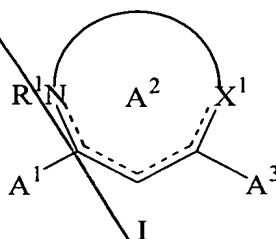
3-(7-[2,2']bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; or

a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

66. A method for treating cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R^1 is hydrogen, (C_{1-6}) alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

X^1 is $-S(O)_n-$, wherein n is 0, 1, or 2;

A^1 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A^1 may be substituted with a group selected from $-R^3$, $-X^2OR^3$, $-X^2C(O)R^3$, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, $-X^2SR^3$, $-X^2S(O)R^3$, $-X^2S(O)_2R^3$, $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)OR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_2R^3$ and $-X^2S(O)_2NR^3R^4$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^3 is $-X^2R^5$ wherein X^2 is as defined above and R^5 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A^1 and R^5 that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or

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halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A¹ and R⁵ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the provisos that only one of A¹ and R⁵ is a fused polycyclic ring system;

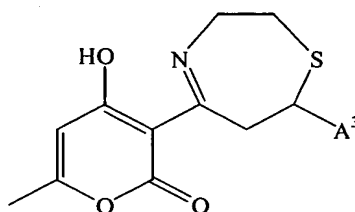
A² is a monocyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A² may be substituted with a group selected from -R⁸, -X²OR⁸, -X²C(O)R⁸, -X²OC(O)R⁸, -X²C(O)OR⁸, -X²SR⁸, -X²S(O)R⁸, -X²S(O)₂R⁸, -X²NR⁴R⁸, -X²NR⁴C(O)R⁸, -X²NR⁴C(O)OR⁸, -X²C(O)NR⁴R⁸, -X²NR⁴C(O)NR⁴R⁸, -X²NR⁴C(NR⁴)NR⁴R⁸, -X²NR⁴S(O)₂R⁸ and -X²S(O)₂NR⁴R⁸, wherein X² is a bond or (C₁₋₆)alkylene, R⁸ is -X²R⁹ wherein X² is as defined above and R⁹ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A² and R⁸ that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²C(O)NR⁴X²C(O)OR⁴, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A² and R⁸ may be substituted further with 1 to 2 groups

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independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the proviso that only one of A² and R⁸ is a fused polycyclic ring system; and

A³ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A³ may be substituted with a group selected from -R⁹, -X³OR⁹, -X²C(O)R⁹, -X²OC(O)R⁹, -X²C(O)OR⁹, -X²SR⁹, -X²S(O)R⁹, -X²S(O)₂R⁹, -X²NR⁴R⁹, -X²NR⁴C(O)R⁹, -X²NR⁴C(O)OR⁹, -X²C(O)NR⁴R⁹, -X²NR⁴C(O)NR⁴R⁹, -X²NR⁴C(NR⁴)NR⁴R⁹, -X²NR⁴S(O)₂R⁹ and -X²S(O)₂NR⁴R⁹, wherein X² is a bond or (C₁₋₆)alkylene, R⁹ is -X²R¹⁰ wherein X² is as defined above and R¹⁰ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A³ and R¹⁰ that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A³ and R¹⁰ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the proviso that only one of A³ and R¹⁰ is a fused polycyclic ring system; or an N-oxide derivative, prodrug

derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof; with the proviso that when said compound is of

Formula II(a):



II(a)

then A³ is other than:

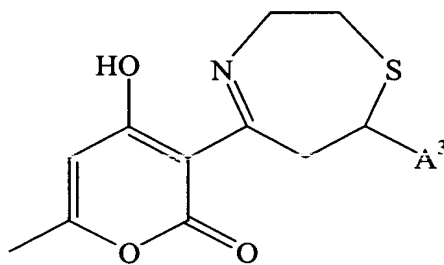
- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl;

and

- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

67. The method of claim 66, with the further proviso that when said compound is Formula II(a):

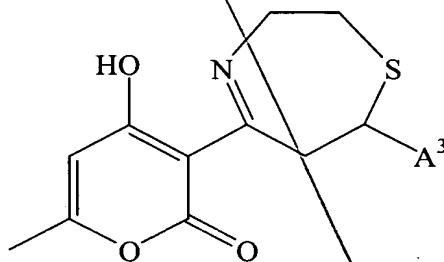


II(a)

then A³ is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl, or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or
a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

68. The method of claim 66, with the further proviso that when said compound is Formula II(a):



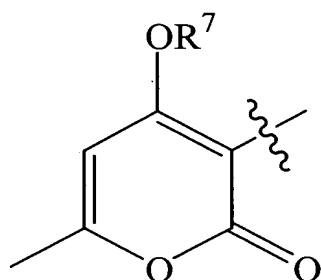
II(a)

then A³ is other than:

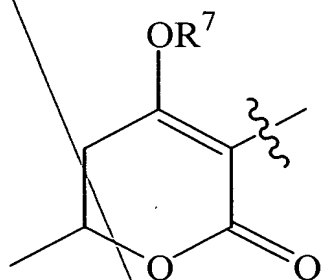
- (a) benzo[1,3]dioxolyl;
(b) 2,3-dihydro-benzo[1,4]dioxinyl; and
(c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C₁₋₆)alkyl; or

a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

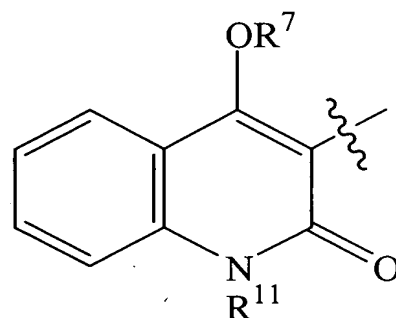
69. The method of Claim 66, wherein A¹ of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):



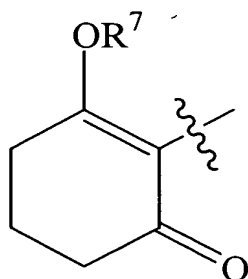
(a)



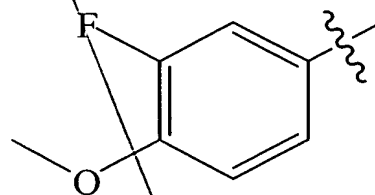
(b)



(c)



(d)



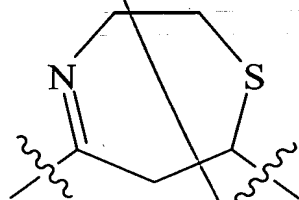
(e)

A¹ 2
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h¹

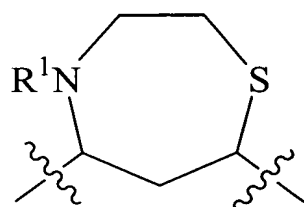
in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valance is attached to A^2 ; and

A^2 of said compound is as defined above or is a group selected from Formulae (h),

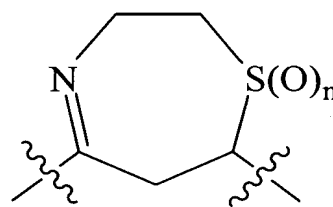
(k), (l) and (m):



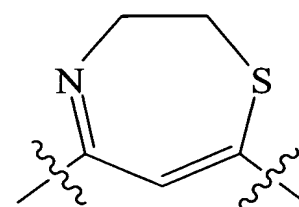
(h)



(k)



(l)



(m)

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl; or a N -oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

70. The method of Claim 69, wherein A^3 of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6}) alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, halo, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and

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$-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

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72. The method of claim 66, wherein said compound is selected from the group consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thiazepin-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-
tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-
hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-
hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-
hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-
tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-
methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-
methyl-pyran-2-one;

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3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

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3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1 λ^4 -[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1 λ^6 -[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

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A13
3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-
pyran-2-one;

3-(7-[2,2']bithienyl-5-yl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-
2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-
enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-
dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual
stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

73. A method for treating cancer, comprising administering to an animal in need
of such treatment an effective amount of a compound selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-
pyran-2-one;

3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-
pyran-2-one;

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-
pyran-2-one;

3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-
methyl-pyran-2-one;

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Sub B1
3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

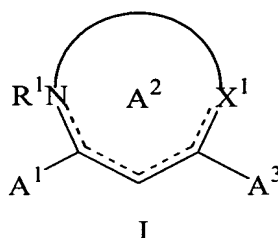
a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

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Sub B1
75. The method of Claims 66 or 73, wherein said cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute and chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides, head and neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell

carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma.

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76. A method for the treatment of drug resistant cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R¹ is hydrogen, (C₁₋₆)alkyl or -C(O)R⁶, wherein R⁶ is as defined below, or R¹ is absent when a double bond exists between the nitrogen atom to which R¹ is attached and an adjacent ring atom or R¹ is as defined below;

X¹ is -S(O)_n-, wherein n is 0, 1, or 2;

A¹ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A¹ may be substituted with a group selected from -R³, -X²OR³, -X²C(O)R³, -X²OC(O)R³, -X²C(O)OR³, -X²SR³, -X²S(O)R³, -X²S(O)₂R³, -X²NR³R⁴, -X²NR⁴C(O)R³, -X²NR⁴C(O)OR³, -X²C(O)NR³R⁴, -X²NR⁴C(O)NR³R⁴, -X²NR⁴C(NR⁴)NR³R⁴, -X²NR⁴S(O)₂R³ and -X²S(O)₂NR³R⁴, wherein X² is a bond or (C₁₋₆)alkylene, R³ is -X²R⁵ wherein X² is as defined above and R⁵ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated,

A/4
Sub
B1

partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A^1 and R^5 that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^1 and R^5 may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the provisos that only one of A^1 and R^5 is a fused polycyclic ring system;

A^2 is a monocyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A^2 and R^8 that contains from 3 to 8 ring atoms may be

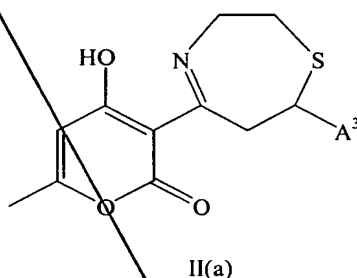
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substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²C(O)NR⁴X²C(O)OR⁴, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A² and R⁸ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the proviso that only one of A² and R⁸ is a fused polycyclic ring system; and

A³ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A³ may be substituted with a group selected from -R⁹, -X²OR⁹, -X²C(O)R⁹, -X²OC(O)R⁹, -X²C(O)OR⁹, -X²SR⁹, -X²S(O)R⁹, -X²S(O)₂R⁹, -X²NR⁴R⁹, -X²NR⁴C(O)R⁹, -X²NR⁴C(O)OR⁹, -X²C(O)NR⁴R⁹, -X²NR⁴C(O)NR⁴R⁹, -X²NR⁴C(NR⁴)NR⁴R⁹, -X²NR⁴S(O)₂R⁹ and -X²S(O)₂NR⁴R⁹, wherein X² is a bond or (C₁₋₆)alkylene, R⁹ is -X²R¹⁰ wherein X² is as defined above and R¹⁰ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A³ and R¹⁰ that contains from 3 to 8 ring atoms may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶,

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$-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$,
 $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$,
 $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is
 (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said carbocycloalkyl and
heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups
independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that
only one of A^3 and R^{10} is a fused polycyclic ring system; or a *N*-oxide derivative, prodrug
derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a
pharmaceutically acceptable salt thereof; with the proviso that when said compound is of
Formula II(a):



II(a)

then A^3 is other than:

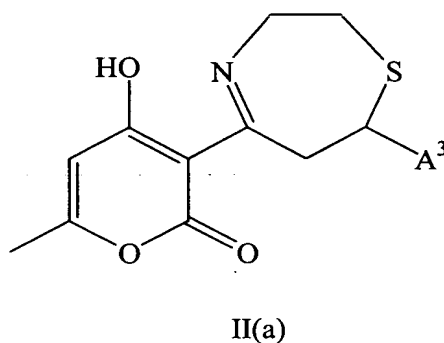
- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl;

and

- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

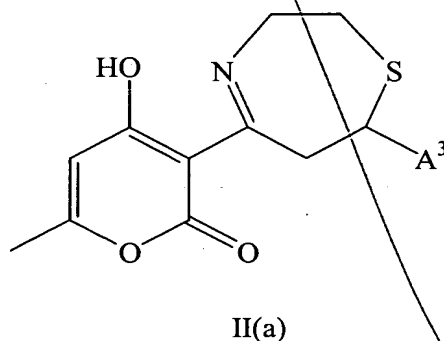
77. The method of claim 76, with the further proviso that when said compound is Formula II(a):



then A³ is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

78. The method of claim 76, with the further proviso that when said compound is Formula II(a):

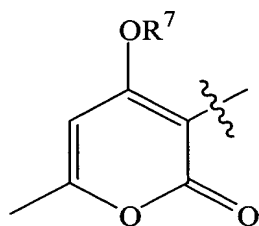


then A³ is other than:

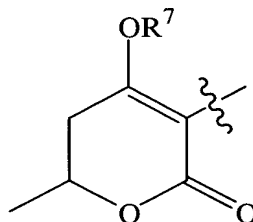
- (a) benzo[1,3]dioxolyl;
(b) 2,3-dihydro-benzo[1,4]dioxinyl; and
(c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C₁₋₆)alkyl; or

a *N*-oxide derivative, prodrug, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

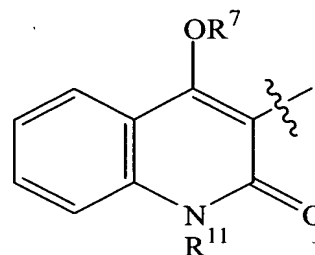
79. The method of Claim 76, wherein A¹ of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):



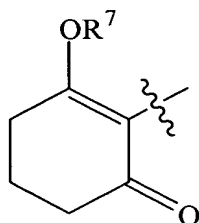
(a)



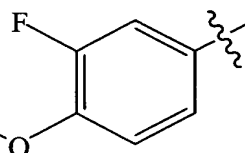
(b)



(c)



(d)

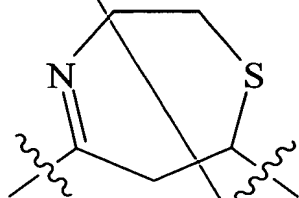


(e)

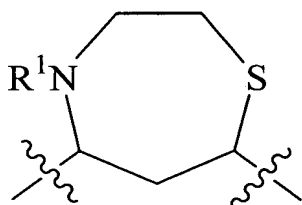
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in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valance is attached to A^2 ; and

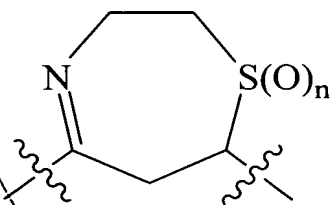
A^2 of said compound is as defined above or is a group selected from Formulae (h), (k), (l) and (m):



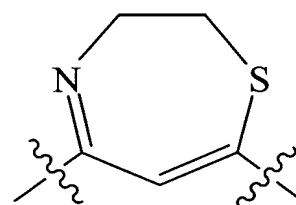
(h)



(k)



(l)



(m)

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

80. The method of Claim 79, wherein A^3 of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6}) alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, halo, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and $-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

82. The method of claim 76, wherein said compound is selected from the group consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thiazepin-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-
pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-
methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfonyl-phenyl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfonyl-phenyl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfonyl-phenyl)-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-
[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-
tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-
hydroxy-6-methyl-pyran-2-one;

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3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

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3-(7-[2,2']bithienyl-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

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4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1H-1 λ^4 -[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1H-1 λ^6 -[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

86. (once amended) The pharmaceutical composition of Claim 55, wherein said cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin,

mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosphamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, imitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, HERCEPTIN (trastuzumab), RITUXAN (rituximab) and alanosine.

Please add the following claims:

94. (new) The compound of any of claims 1, 47, 48, 51, wherein said prodrug derivative is an ester of a compound comprising a hydroxy group or a carboxy group.

95. (new) The pharmaceutical composition of claim 54, wherein said prodrug derivative is an ester of a compound comprising a hydroxy group or a carboxy group.

96. (new) The method of any one of claims 57, 64, 66, 73, 76, and 83, wherein said prodrug derivative is an ester of a compound comprising a hydroxy group or a carboxy group.

97. (new) The method of claims 57 or 64, wherein said disorder responsive to the induction of apoptosis is inflammation, inflammatory bowel disease, psoriasis, an autoimmune disease selected from the group consisting of rheumatoid arthritis, multiple sclerosis, diabetes mellitus, Hashimoto's thyroiditis, and autoimmune lymphoproliferative syndrome, or a cancer selected from the group consisting of Hodgkin's disease,

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non-Hodgkin's lymphoma, acute and chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides, head and neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma.